DOCKET NO.: ISIS-5300



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Brenda F. Baker, et al. Confirmation No.: 7033

Application No.: 10/701,265 Group Art Unit: 1635

Filing Date: November 4, 2003 Examiner: Not Yet Assigned

For: 2'-METHOXY SUBSTITUTED OLIGOMERIC COMPOUNDS AND

COMPOSITIONS FOR USE IN GENE MODULATIONS

DATE OF DEPOSIT: Opril 28, 2004

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID, ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE UNITED STATES PATENT AND TRADEMARK OFFICE, P.O. BOX 1450, ALEXANDRIA,

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Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of

the above identified application as set forth in § 1.491, before the mailing date
of a first Office Action on the merits of the above-identified application, or
before the mailing date of a first Office Action after the filing of request for
continued examination under § 1.114, no additional fee is required.
In accordance with § 1.129(a), this Information Disclosure Statement is being
filed in connection with \square the first or \square second After Final Submission,
therefore:
Certification in Accordance with § 1.97(e) is attached; or
The fee of \$180.00 as set forth in § 1.17(p) is attached.
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of the Issue Fee, therefore included are: Certification in Accordance with §
1.97(e); and the submission fee of \$180.00 as set forth in § 1.17(p).
Copies of each of the references listed on the attached Form PTO-1449 are
enclosed herewith.

- Copies of references listed on the attached Form PTO-1449 are enclosed herewith
- Copies of references listed on the attached Form PTO 1449 are not required to be submitted pursuant to the June 30, 2003 recent revisions to 37 CFR § 1.98(a)(2)(i).

EXCEPT THAT:

- In view of the voluminous nature of references 3, 16, 23-25, and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.
- In accordance with § 1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C.§ 120 have been made in the instant application:
 - Copies of references 3-28, 156-183 and 209-215 listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No. 08/659,440, filed June 6, 1996 now U.S. Patent No. 5,898,031; copies of references 29-112, 184-192 and 216-217 listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No. 08/870,608, filed June 6, 1997 now U.S. Patent No. 6,107,094; copies of references 113-129, 193-195 and 218 listed on the attached Form PTO-1449 were

previously cited by or submitted to the Patent and Trademark Office in prior Application No. 09/479,783, filed January 7, 2000.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

The relevance of those listed references which are not in the English language is as follows:

There are no listed references which are not in the English language.

Date: April 28, 2004

John A. Harrelson, Jr. Registration No. 42,637

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Form PTC	D-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265	
Cited	nt and Publications by Applicant sheets if necessary)	Applicant Brenda F. Baker, et a	ıl.	
	ment of Commerce Trademark Office	Filing Date November 4, 2003	Group 1635	
		Confirmation No. 7033		
ОТНЕ	ER DOCUMENTS (Inclu	ding Author, Title, Da	te, Pertinent Pages, Etc.)	
3	Ausubel, et al., Eds., Cu New York	urrent Protocols in Mole	ecular Biology, 1988, Wiley & Sons,	
4	Beaucage S. and Iyer, R phosphoramidite approa		thesis of oligonucleotides by the rs, 1992, 48, 2223-2311	
5	 Beaucage S. and Iyer, R., "The synthesis of modified oligonucleotides by the phosphoramidite approach and their applications", Tetrahedron, 1993, 49, 6123-61 Bhat, et al., "A Simple and Convenient Method for the Selective N-Acylations of Cytosine Nucleosides", Nucleosides and Nucleotides, 1989, 8, 179-183 			
7	7 Crooke, S.T. and Bennett, C.F., "Progress in Antisense Oligonucleotide Therapeutics", Annu. Rev. Pharmacol. Toxicol., 1996, 36, 107-129			
8	Crooke, et al., "Kinetic characteristics of Escherichia coli Rnase H1: cleavage of various antisense oligonucleotide-RNA duplexes", <i>Biochem. J.</i> , 1995 , <i>312</i> , 599-60			
9	Dagle, et al., "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: studies of An2 and cyclin in embryogenesis" Nucleic Acids Research, 1990, 18, 4751-4757 Dagle, et al., "Pathways of Degradation and Mechanism of Action of Antisense Oligonucleotides in Xenopus laevis Embryos", Antisense Res. And Dev., 1991, 1, 11 20			
10				
11	Dagle, et al., "Physical properties of oligonucleotides containing phosphoramidate-modified internucleoside linkages", Nucleic Acids Research, 1991, 19, 1805-1810			
12	Englisch, U. And Gauss, D.H., "Chemically Modified Oligonucleotides as Probes and Inhibitors", Angewandt Chemie, International Edition Engl., 1991, 30, 613-629			
EXAMINER		DATE C	ONSIDERED	

^{*} A copy of this reference will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.

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Form	PTO	-1449 Modified	Docket No ISIS-5300		Application No. 10/701,265
C	Cited b	t and Publications by Applicant cheets if necessary)	Applicant Brenda F.	Baker, et al.	
		nent of Commerce Trademark Office	Filing Dat November		Group 1635
			Confirmat 7033	ion No.	
O	THE	R DOCUMENTS (Includ	ing Author	, Title, Date, l	Pertinent Pages, Etc.)
	13		s yields pol		ligonucleotides complementary to edetermined length", Nucleic
	14	1	Eder, P.S. and Walder, J.A., "Ribonuclease H from K562 Human Erythroleukemia Cells", J. Biol. Chem., 1991, 266, 6472-6479		
	15	Kawasaki, et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets", J. Med. Chem., 1993, 36, 831-841			
*	16	Kawasaki, et al., "Synthesis and Biophysical Studies of 2'-dRIBO-2'-F Modified Oligonucleotides", ISIS Pharmaceuticals, Inc., 2280 Faraday Avenue, Carlsbad, CA 92008, USA			
	Martin, "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", Helv. Chim. Acta., 1995, 78, 486-504			_	
Monia, et al., "Selective Inhibition of Mutant Ha-ras mRNA Expression by Antisense Oligonucleotides", J. Biol. Chem., 1992, 267, 19954-19962					
	Monia, et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", J. Biol. Chem., 1993, 268, 14514-14522				
	20	Reese, C.B., et al., "4-(1,2,4-Triazol-1-yl)-and 4-(3-Nitro-1,2,4-triazol-1-yl)-1-(β-D-Arabinofuranosyl)cytosine(Ara-C)", J. Chem. Soc. Perkin Trans. I, 1982, pgs. 1171-1176			
	21	Robins, et al., "Nucleic acid related compounds. 41. Restricted furanose conformations of 3',5'-O(1,1,3,3-tetraisoprpyldisilox-1,3-diyl)nucleosides provide a convenient evaluation of anomeric configuration ^{1,2} ", Can. J. Chem., 1983, 61, 1911-1920			
	Saison-Behmoaras, T., et al., "Short modified antisense oligonucleotides directed against Ha ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", <i>EMBO</i> , 1991 , <i>10</i> , 1111-1118				
EXAMINER				DATE CON	SIDERED

^{*} A copy of this reference will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.

	Form PTO-1449 Modified Docket No. Application No.						
Form I	PTO	-1449 Modified	ISIS-5300		10/701,265		
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1	-	nent of Commerce Trademark Office	Filing Dat November		Group 1635		
			Confirmat 7033	ion No.			
O 7	THEF	R DOCUMENTS (Includ	ing Author	, Title, Date, l	Pertinent Pages, Etc.)		
*	23	Concise Encyclopedia of Kroschwitz, J.I., Ed., Joh	•	_	gineering, pgs. 858-859,		
*	24	Oligonucleotide Synthes	is, A Practio	cal Approach, l	M.J. Gait, Ed., IRL Press, 1984		
*	25	Oligonucleotide and Analogs, A Practical Approach, F. Eckstein, Ed., IRL Press, 1991, Chapters 1-7					
	26	De Mesmeker, et al., "Antisense Oligonucleotides", Acc. Chem. Res., 1995, 28, 366-374					
	Sands, et al., "Biodistribution and Metabolism of Internally ³ H-Labeled Olionucleotides. II. 3',5'-Blocked Oligonucleotides", <i>Am. Soc. Pharmacol. Exp. Ther.</i> , 1995 , <i>47</i> , 636-646						
	Strickland, et al., "Antisense RNA Directed Against the 3' Noncoding Region Prevents Dormant mRNA Activation in Mouse Oocytes", Science, 1988, 241, 680-684						
	Goodchild, et al., "Conjugates of Oligonucleotides and Modified Oligonucleotides: A Review of their Synthesis and Properties", <i>Bioconjugate Chem.</i> , 1990, 1(3), 165-187						
	30	30 Menelev, et al., <i>Bioorg. & Med. Chem. Lett.</i> , 1994 , 4(24), 2929-2934					
	31	Lengyel, J. Enzym. Res., 1987, 7, 511-519					
	32 Milligan, J. Med. Chem., 1993, 36, 1923						
EXAMINER				DATE CON	SIDERED		

^{*} A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since they are believed to be too voluminous and easily obtainable by the Examiner.

Form I	Form PTO-1449 Modified Docket No. ISIS-5300 Application No. 10/701,265					
C	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)			Baker, et al.		
		nent of Commerce Trademark Office	Filing Dat November		Group 1635	
			Confirmat 7033	ion No.		
OT	THE	R DOCUMENTS (Includ	ling Author	, Title, Date,	Pertinent Pages, Etc.)	
	33	Tseng, et al., "Antisense Therapeutics", Cancer G			gy in the Development of Cancer , 65-71	
	34	Westermann, et al., "Inhantisense oligodeoxyribo			740 virus large T-antigen by <i>Acta.</i> , 1989 , <i>48</i> , 85-93	
	Stein, C.A. et al., "Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?", Science, 1993, 261, 1004-1012					
	 Stull, et al., "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress ar Prospects", <i>Pharm. Res.</i>, 1995, <i>Pharm. Rev.</i>, 12, 465-482 Uhlmann, et al., "Antisense Oligonucleotides: A New Therapeutic Principle", C Rev., 1990, 90, 543 			• •		
				ew Therapeutic Principle", Chem.		
	Akashi, et al., "Novel Stationary Phases for Affinity Chromatography. Nucleoble Selective Recognition of Nucleosides and Nucleotides on Poly(9-vinyladenine) Supported Silica Gel ¹⁾ ", Chem. Letters, 1988, 1093-1096			ides on Poly(9-vinyladenine)-		
	 Alberts, et al., "DNA-Cellulose Chromatography", Meth. Enzymol., 1971, 21, 198-217 Arndt-Jovin, et al., "Covalent Attachment of DNA to Agarose", Eur. J. Biochem., 1975, 54, 411-418 Blanks, et al., "An oligodeoxynucleotide affinity column for the isolation of sequence specific DNA binding proteins", Nucleic Acids Res., 1988, 16, 10283-10299 			omatography",	Meth. Enzymol., 1971, 21, 198-	
				to Agarose", Eur. J. Biochem.,		
	Blomberg, P., "Control of replication of plasmid R1: the duplex between the antisense RNA, CopA, and its target, CopT, is processed specifically <i>in vivo</i> and <i>in vitro</i> by Rnase III", <i>EMBO J.</i> , 1990 , <i>9</i> , 2331-2340			cessed specifically in vivo and in		
EXAMINER				DATE CON	SIDERED	
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Form PTO	-1449 Modified	Docket No ISIS-5300		Application No. 10/701,265
List of Paten Cited b (Use several s	Applicant Brenda F.	Baker, et al.		
	nent of Commerce Frademark Office	Filing Dat November		Group 1635
		Confirmat 7033	ion No.	
ОТНЕ	R DOCUMENTS (Includ	ding Author	, Title, Date,	Pertinent Pages, Etc.)
43				A to macroporous supports: I. eic Acids Res., 1982, 10, 7163-
44				
45	Chodosh, et al., "A Single Polypeptide Possesses the Binding and Transcription Activities of the Adenovirus Major Late Transcription Factor", <i>Mol. Cell. Biol.</i> , 1986 , <i>6</i> , 4723-4733			
46	Crooke, et al., "Phmarmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", J. Pharmacol. Exp. Therm., 1996, 277, 923-927			
47	47 Dake, et al., "Purification and Properties of the Major Nuclease from Mitochondria Saccharomyces cerevisiae", J. Biol. Chem., 1988, 263, 7691-7702			·
Day, et al., "Immobilization of polynucleotides on magnetic particles", Biochem. J. 1991, 278, 735-740				magnetic particles", Biochem. J.,
Drmanac, et al., "DNA Sequence Determination by Hybridization: A Strategy for Efficient Large-Scale Sequencing", Science, 1993, 260, 1649-1652			· · · · · · · · · · · · · · · · · · ·	
50	Duncan, et al., "Affinity Chromatography of a Sequence-Specific DNA Binding Protein Using Teflon-Linked Oligonucleotides", Anal. Biochem., 1988, 169, 104-10			-
51	Dunn, J.J. and Studier, F.W., "Effect of RNAase III Cleavage on Translation of Bacteriophage T7 Messenger RNAs", J. Mol. Biol., 1975, 99, 487-499			_
52	Elela, et al., "RNase III Cleaves Eukaryotic Preribosomal RNA at a U3 snoRNP-Dependent Site", Cell, 1996, 85, 115-124			
EXAMINER			DATE CON	SIDERED

 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction 	Form 1	Form PTO-1449 Modified Docket No. ISIS-5300 Application No. 10/701,265				
Patent and Trademark Office November 4, 2003 Confirmation No. 7033 OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) 53 Fahy, et al., "Design and synthesis of polyacrylamide-based oligonucleotide supports for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826 54 Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342 55 Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 56 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor ranew purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SmB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction	C	Cited by Applicant			Baker, et al.	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) 53 Fahy, et al., "Design and synthesis of polyacrylamide-based oligonucleotide supports for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826 54 Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342 55 Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 56 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor reanew purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction						
53 Fahy, et al., "Design and synthesis of polyacrylamide-based oligonucleotide supports for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826 54 Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342 55 Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 56 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor to a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction					ion No.	
for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826 54 Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342 55 Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 56 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor vanew purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction	O	THE	R DOCUMENTS (Inclu	ding Author	, Title, Date,	Pertinent Pages, Etc.)
55 Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 56 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor ranew purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		53		•		_
 Fodor, et al., "Eight-Directed, spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773 Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor r. a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction 		54		Affinity Chro	matography",	Methods Enzymol., 1990, 184,
Solfataricus", Eur. J. Biochem., 1993, 16, 305-310 57 Gabrielsen, et al., "Magnetic DNA affinity purification of yeast transcription factor to a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis,				le Parallel Chemical Synthesis",
Gabrielsen, et al., "Magnetic DNA arimity purification of yeast transcription factor to a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267 58 Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		Fusi, et al., "Ribonucleases inc				nophilic archaebacterium S.
with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438 59 Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		a new purification principle for the ultrarapid isolation of near homogeneous facto				· -
Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47 60 Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 61 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 62 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		58	Goenie, "Trypanosoma brucei: Calcium-Dependent Endonbonuclease is Associated			
Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649 Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction		Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. <i>Biochem. Parasitol.</i> , 1985 , <i>15</i> , 37-47				
Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391 Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction	·	Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA				
covalent attachment of DNA to cellulose. Application for hybridization-restriction		61	Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids			
analysis and for <i>in vitro</i> synthesis of DNA probes", <i>Nucleic Acids Res.</i> , 1986 , <i>14</i> , 9171-9191		62	covalent attachment of DNA to cellulose. Application for hybridization-restriction analysis and for <i>in vitro</i> synthesis of DNA probes", <i>Nucleic Acids Res.</i> , 1986, 14,			
EXAMINER DATE CONSIDERED	EXAMINER				DATE CON	SIDERED

Form PTO-	-1449 Modified	Docket No ISIS-5300		Application No. 10/701,265
Cited b	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)			
	nent of Commerce Frademark Office	Filing Dat November		Group 1635
		Confirmat 7033	ion No.	
ОТНЕ	R DOCUMENTS (Includ	ling Author	, Title, Date, l	Pertinent Pages, Etc.)
63	Goss, T.A. and Bard, M. Chromatogr., 1990, 508,		formance affini	ty chromatography of DNA", J.
64	Guo, et al., "Direct fluorescence analysis of genetic polymorphisms by hybridization with oligonucleotide arrays on glass supports", Nucl. Acids Res., 1994, 22, 5456-5465			
65	 Kadonaga, J.T. and Tjian, R., "Affinity purification of sequence-specific DNA binding proteins", <i>Proc. Natl. Acad. Sci. USA</i>, 1986, 83, 5889-5893 Kadonaga, J.T., "Purification of Sequence-Specific Binding Proteins b DNA Afficheromatography", <i>Methods in Enzymology</i>, 1991, 208, 10-23 			
66				•
67	Kasher, et al., "Rapid Enrichment of HeLa Trancription Factors IIIB and IIIC by Using Affinity Chromatography Based on Avidin-Biotin Interactions", Mol. And Cell. Biol., 1986, 6, 3117-3127			·
68	Kawaguchi, et al., "Purification of DNA-binding transcription factors by their selective adsorption of the affinity atex particles", <i>Nucleic Acids Research</i> , 1989 , 6229-6240			_
69	Kennedy, "Hydrophobic Chromatography", Methods in Enzymology, 1990, 182, 339			
70	Background, Principles, and a Summary of Results Obtained with Myosin Heavy Chain", Cell Motil. and Cytoskel., 1989, 14, 92-102			Obtained with Myosin Heavy
71	murine erythroleukemia	cells induce	ed to differentia	lved in p53 mRNA maturation in ate", <i>EMBO J.</i> , 1989 , <i>8</i> , 4107-4114
72	Krinke, L. And Wulff, D mediated by λ OOP antis			ybrolysis of λcII-O gene mRNA vel., 1990, 4, 2223-2233
EXAMINER		!	DATE CON	SIDERED

Form PTO-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265		
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant Brenda F. Baker, e	t al.		
U.S. Department of Commerce Patent and Trademark Office	Filing Date November 4, 2003	Group 1635		
	Confirmation No. 7033			
OTHER DOCUMENTS (Includ	ling Author, Title, l	Date, Pertinent Pages, Etc.)		
Krystal, et al., "N-myc m Antisense Transcripts", A		A-RNA Duplex with Endogenous 1990, 10, 4180-4191		
75 Lohrmann, et al., "New S	Solid Supports for D	NA Synthesis" <i>DNA</i> , 1984 , <i>3</i> , 122		
	ads™, and the chara	alent binding of nucleic acids to cteristics of the bound nucleic acids in 988 , <i>16</i> , 10861-10880		
1 1	which controls permanent expression of a Dictyostelium gene", Nucl. Acids Res			
78 Matson, et al., "Biopolyr 1994, 217, 306-310	ypropylene Supports", Anal. Biochem.,			
novel linker for oligonuc	eleotide synthesis and	eotide hybridisations on glass supports: a d hybridisation properties of lcids. Res., 1992, 20, 1679-1684		
Meegan, J.M. and Marcus, P.I., "Double-Stranded Ribonuclease Coinduced wi Interferon", <i>Science</i> , 1989 , <i>244</i> , 1089-1091				
	Narhi, et al., "Hydrophobic Interaction Chromatography in Alkaline pH", Anal. Biochem., 1989, 182, 266-270			
82 Nellen, W., C., "What m 1993, 18, 419-424	82 Nellen, W., C., "What makes an mRNA anti-sense-itive?", Curr. Opin. Cell. Biol.,			
EXAMINER	DATE	CONSIDERED		

Form PTO	-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265	
Cited b	at and Publications by Applicant sheets if necessary)	Applicant Brenda F. Baker, et al.		
	nent of Commerce Frademark Office	Filing Date November 4, 2003	Group 1635	
		Confirmation No. 7033		
OTHE	R DOCUMENTS (Includ	ling Author, Title, Date,	Pertinent Pages, Etc.)	
83		anisms of gene regulation A", Biochem., Soc. Trans	by endogenous and artificially s., 1992 , <i>20</i> , 750-754	
84	1	Nitta, et al., "Purification and Some Properties of Ribonuclease from Xenopus laevis Eggs", Biol. Pharm. Bull. (Jpn.), 1993, 16, 353-356		
85	Noguchi, et al., "Characterization of an Antisense Inr Element in the eIF-2α Gene", J. Biol. Chem., 1994, 269, 29161-29167			
86	Noyes, et al., "Nucleic Acid Hybridization Using DNA Covalently Coupled to Cellulose", Cell, 1975, 5, 301-310			
87	Pease, et al., "Light-generated oligonucleotide arrays for rapid DNA sequence analysis", <i>Proc. Natl. Acad. Sci. USA</i> , 1994 , <i>91</i> , 5022-5026			
88	Pon, et al., "Derivatization of Controlled Pore Glass Beads for Solid Phase Oligonucleotide Synthesis", <i>BioTech.</i> , 1988 , <i>6</i> , 768-773			
89	Prokipcak, et al., "Purification and Properties of a Protein that Binds to the C-terminal Coding Region of Human c-myc mRNA", J. Biol. Chem., 1994, 269, 9261-2969			
90	Saito, H. And Richardson, C., "Processing of mRNA by Ribonuclease III Regulates Expression of Gene 1.2 of Bacteriophage T7", 1981 , <i>Cell</i> , <i>27</i> , 533-542			
91	Schott, "Template-Chromatographie An Stationar Gebundenen Oligonukleotiden", J. Chromatogr., 1975, 115, 461-476			
92	92 Seliger, H., "Handelsubliche Polymere als Trager in der Oligonucleotidsynthese, 1", Die Makromolekulart Chemie, 1975, 176, 1611-1627			
EXAMINER		DATE CON	ISIDERED	

Form PT	O-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265	
Cited	ent and Publications by Applicant I sheets if necessary)	Applicant Brenda F. Baker, et al.		
	tment of Commerce Trademark Office	Filing Date November 4, 2003	Group 1635	
		Confirmation No. 7033		
ОТНІ	ER DOCUMENTS (Incl	uding Author, Title, D	ate, Pertinent Pages, Etc.)	
9:	Senger, H., and Aumai	lalkohol und N-Vinylpy	cleotidsynthese an unvernetzten yrrolidon", Die Makromolekulare	
94	Seliger, H. And Aumar		Synthesis on a Polymer Support Letters, 1973, No. 31, 2911-2914	
9:	Siddell, S.G., "RNA H	Sur. J. Biochem., 1978, 92, 621-629		
90	at the 5' terminus: synt	thesis of oigonucleotides containing an aliphatic amino group thesis of fluorescent DNA primers for use in DNA sequence <i>Res.</i> , 1985 , <i>13</i> , 2399-2412		
9′	Stolat, P. And Zillig, V	W., "Antisense RNA mediates transcriptional processing in an eating a novel kind of RNase activity", <i>Mol. Microbiol.</i> , 1993 , tification of polymerase chain reaction products by affinity-n", <i>Nucl. Acids Res.</i> , 1988 , <i>16</i> , 11327-11338		
98	Syvanen, et al., "Quant			
99	Szyi, et al., "Growth R	egulation of Mouse DN Them., 1991, 266, 10027	A Methyltransferase Gene -10030	
100	McBride, L.J. and Car	ruthers, M.H., "An Investigation of Several Deoxynucleoside of synthesizing Deoxyoligonucleotides", <i>Tetrahedron</i> 248		
10	Van Ness, et al., "A versatile solid support system for oligodeoxynucleotide probased hybridization assays", <i>Nucleic Acids Research</i> , 1991 , <i>19</i> , 3345-3350 Volk, et al., "An antisense transcript from the Xenopus laevis bFGF gene coding an evolutionariy conserved 24 kd protein", <i>EMBO J.</i> , 1989 , <i>8</i> , 2983-2988			
102				
EXAMINER		DATE C	CONSIDERED	

List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office Piling Date November 4, 2003 Confirmation No. 7033 OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) Wetlaufer, et al., "Surfactant-Mediated Protein Hydrophobic-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60 Wu, et al., "Purification and Properties of Drosophila Heat Shock Activator Protein Science, 1987, 238, 1247-1253 Wu, et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47 106 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 108 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	Form PTC	0-1449 Modified	Docket No ISIS-5300		Application No. 10/701,265		
Patent and Trademark Office November 4, 2003 1635	Cited	by Applicant		Baker, et al.			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) 103 Wetlaufer, et al., "Surfactant-Mediated Protein Hydrophobic-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60 104 Wu, et al., "Purification and Properties of Drosophila Heat Shock Activator Protein Science, 1987, 238, 1247-1253 105 Wu, et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47 106 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 2arytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 110 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23			_		_		
103 Wetlaufer, et al., "Surfactant-Mediated Protein Hydrophobic-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60 104 Wu, et al., "Purification and Properties of Drosophila Heat Shock Activator Protein Science, 1987, 238, 1247-1253 105 Wu, et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47 106 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 108 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 110 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23			l .	ion No.			
Wetaurer, et al., "Surfactant-Mediated Protein Hydrophoto-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60 104 Wu, et al., "Purification and Properties of Drosophila Heat Shock Activator Protein Science, 1987, 238, 1247-1253 105 Wu, et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47 106 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 108 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 110 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	ОТНЕ	R DOCUMENTS (Includ	ling Author	, Title, Date, 1	Pertinent Pages, Etc.)		
 Wu, et al., "Purification and Properties of Drosophila Heat Shock Activator Protein Science, 1987, 238, 1247-1253 Wu, et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23 	103	wetlaufer, et al., "Surfac		•	•		
Mucromolecules", Methods in Enzymology, 1996, 270, 27-47 106 Yashima, et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119 107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	104	Wu, et al., "Purification	and Propert				
107 Yasuda, et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529 108 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 109 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 110 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	105	wu, et al., "High Resolu		•	•		
spleen", Eur. J. Biochem., 1990, 191, 523-529 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	106	nucleic acid analogue im					
 Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218 Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23 	107	· · · · · · · · · · · · · · · · · · ·					
3'-ends of synthetic oligodeoxyribonucleotides", Nucleic Acids Research, 1987, 15, 5305-5321 Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties an Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	108	Zarytova, et al., "Alfinity			• • • •		
Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23	109	3'-ends of synthetic oligo					
111 Agrawal, S. et al., "Synthesis and Anti-HIV Activity of Oligoribonucleotides and	Hyrup, B. And Meisen, P., "Peptide Nucleic Acids (PNA): Synthesis, Prop						
Their Phosphorothioate Analogs," Ann. N.Y. Acad. Sci., 1992, 2-10	111						
Shibahara, S. et al., "Inhibition of human immunodeficiency virus (HIV-1) replication by synthetic oligo-RNA derivatives," <i>Nucl. Acids Res.</i> , 1989 , <i>17(1)</i> , 239 252	112	• • • • • • • • • • • • • • • • • • • •					
EXAMINER DATE CONSIDERED	EXAMINER	-		DATE CON	SIDERED		

Form PTO-	-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265				
Cited b	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)						
	ent of Commerce rademark Office	Filing Date November 4, 2003	Group 1635				
		Confirmation No. 7033					
ОТНЕК	R DOCUMENTS (Includ	ling Author, Title, Date,	Pertinent Pages, Etc.)				
113	Agrawal, S., "Antisense 1996, 14, 376-388	Oligonucleotides: Towar	ds Clinical Trials," TIBTECH,				
114		Branch, A., "A Good Antisense is Hard to Find," TIBS, 1998, 23, 45-50					
115	Metelev, et al., "Study of antisense oligonucleotide phosphorothioates containing segments of oligodeoxynucleotides and 2'-methyloligoribonucleotides", <i>Bioorg. & Med. Chem. Lett.</i> , 1994 , <i>4</i> , 2929-2934						
116							
117	Ohtsuki, et al., "Isolation thymus", J. Biol. Chem.,	-	le-stranded ribonuclease from calf				
118	Arya, S. K. et al., "Inhibi	ition of RNA Directed Di-Alkylated Polyadenylic	NA Polymerase of Murine Acids," <i>Biochemical and</i> (2), 608-615				
119	Arya, S. K. et al., "Inhibition of Synthesis of Murine Leukemia Virus in Cultured Cells by Polyribonucleotides and Their 2'-O-Alkyl Derivatives," <i>Molecular Pharmacology</i> , 1976 , <i>12</i> , 234-241						
120	Hobbs, J. et al., "Polynucleotides Containing 2'-Amino 2'-deoxyribose and 2'-Azido-2'-deoxyribose [†] ," <i>Biochem.</i> , 1973 , <i>12</i> , 5138-5145						
121	Hobbs, J. et al., "Poly 2'-Deoxy-2'-Aminouridylic Acid, 1972, 46(4), 1509-1515						
122	Hobbs, J. et al., "Polynucleotides Containing 2'-Chloro-2'-deoxyribose," <i>Biochem.</i> , Eckstein et al., Ed., 1972, 11, 4336-4344						
EXAMINER							

Form PTC	Form PTO-1449 Modified			Application No. 10/701,265		
Cited	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)					
	ment of Commerce Trademark Office	Filing Dat November		Group 1635		
		Confirmat 7033	ion No.			
ОТНЕ	R DOCUMENTS (Includ	ding Author	, Title, Date,	Pertinent Pages, Etc.)		
123	123 Wincott et al., "Synthesis, deprotection, ribozymes," Nucl. Acids Res., 1995, 23			on, analysis and purification of RNA and 23(14), 2677-2684		
124	DeClercq, E. et al., "Influence of various 2- and 2'-substituted polyadenyl acids on murine leukemia virus reverse transcriptase," <i>Cancer Letters</i> , 1979 , 7, 27-37					
125		Pieken, W. et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science, 1991, 253, 314-317				
126	Pilet, J. et al., "Structura	•	_	double helical nun, 1973 , <i>52(2)</i> , 517-523		
127	Rottman, F. et al., "Poly by Polynucleotide Phosp			0-Methyladenosine. I. Synthesis 7, 2634-2641		
128	Rottman, F. et al., "Poly Heteropolymers," Bioch			hylnucleotides. II. Synthesis of		
129	polynucleotide structure	," Biochem I	Biophys Res C	d and the role of the 2'-hydroxyl in commun, 1969 , 37(6), 895-901		
130	interference in Drosophi					
131	Biophysica Acta, 2002,	<i>1575</i> , 15-25		nterference," Biochimica et		
132	Carmell, M.A., et al., "the argonaute family: tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis," Genes and Development, 2002, 16, 2733-2742					
EXAMINER		DATE CON	SIDERED			

Form PTO-	Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		Application No. 10/701,265		
Cited by					
	ent of Commerce rademark Office	Filing Date November 4, 2003	Group 1635		
		Confirmation No. 7033			
OTHER	DOCUMENTS (Includ	ling Author, Title, Date	, Pertinent Pages, Etc.)		
133	Chiu, YL., et al., "RNAi in human cells: basic structural and functional feature small interfering RNA," <i>Molecular Cell</i> , September 2002 , <i>10</i> , 549-561				
134	Cogoni, C., et al., "Post-transcriptional gene silencing across kingdoms," Curr. Opinion in Genes Dev., 2000, 10, 638-643				
135	Elbashir, S.M., et al., "Functional anatomy of siRNAs for mediating efficient RNAi in <i>Drosophila melanogaster</i> embryo lysate," <i>EMBO J.</i> , 2001 , <i>29(23)</i> , 6877-6888				
136	Elbashir, S.M., et al., "R RNA's," Genes & Dev.,		ated by 21- and -22-nucleotide		
137	Elbashir, S.M., et al., "D in cultured mammalian c		RNAs mediate RNA interference 001 , 411, 494-498		
138		nd specific genetic interf	erence by double-stranded RNA in		
139	Guo, S., et al., "par-1, a	gene required for establi tive Ser/Thr kinase that	shing polarity in C. elegans is asymmetrically distributed," Cell,		
140	Gura, T., "A silence that	speaks volumes," Natur	re, April 20, 2000 , <i>404</i> , 804-808		
141	Jorgensen, R.A., et al., "Chalcone sythase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense contructs and single-copy vs. complex T-DNA sequences," <i>Plant Mol. Biol.</i> , 1996 , <i>31</i> , 957-973				
142					
EXAMINER		DATE CO	NSIDERED		

Form PTO	-1449 Modified	Docket No. ISIS-5300	Application No. 10/701,265			
Cited b	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		al.			
	nent of Commerce Frademark Office	Filing Date November 4, 2003	Group 1635			
		Confirmation No. 7033				
ОТНЕ	R DOCUMENTS (Includ	ling Author, Title, Da	ate, Pertinent Pages, Etc.)			
143	Martinez, J., et al., "Sing RNAi," Cell, September		siRNAs guide target RNA cleavage in			
144	Mellitzer, G., et al., "Spatial and temporal 'knock down' of gene expression by electroporation of double-stranded RNA and morpholinos into early postimplantation mouse embryos," <i>Mechanisms of Development</i> , 2002, 118, 57-63					
145	Montgomery, M.K., et al., "RNA as a target of double-stranded RNA-mediated genetic interference in <i>Caenorhabditis elegans</i> ," <i>Proc. Natl. Acad. Sci. USA</i> , December 1998, 95, 15502-15507					
146	Napoli, C., et al., "introduction of a chimeric chalcone synthase gene into petunia results in reversible co-suppression of homologous genes in trans," Plant Cell, April 1990, 2, 279-289					
147	Nishikura, K., "A short p key catalyst," Cell, Nove	•	A-directed RNA polymerase acts as a 415-418			
148			RNA trigger: differential requirement e," <i>Molecular Cell</i> , November 2000 , 6,			
149	Schwarz, D.S., et al., "Evidence that siRNAs function as guides, not primers, in the <i>Drosophila</i> and human RNAi pathways," <i>Molecular Cell</i> , September 2002 , <i>10</i> , 537-548					
150	silencing," Cell, Novemb	ber 16, 2001 , <i>107</i> , 465				
151	October 16, 1998, 282, 4	30-431	ig in the genome sequence," Science,			
152			4-dependent gene silencing triggered in January 25, 2002 , <i>295</i> , 694-697			
EXAMINER	AMINER DATE CONSIDERED					

Form	Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		Docket N ISIS-5300		Application No. 10/701,265		
C			Applicant Brenda F. Baker, et al.				
	U.S. Department of Commerce Patent and Trademark Office			te r 4, 2003	Group 1635		
				tion No.			
O	THEF	R DOCUMENTS (Inclu	ding Autho	r, Title, Date,	Pertinent Pages, Etc.)		
	153	Timmons, L., et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interferences in <i>Caenorhabditis elegans</i> ," <i>Gene</i> , 2001 , <i>263</i> , 103-112					
	154	Timmons, L., et al., "Sp 1998, 395, page 854	pecific interf	erence by inge	sted dsRNA," Nature, October 29,		
	155	Tuschl, T., et al., "Targo Genes & Dev., 1999, 13			y double-stranded RNA in vitro,"		
	-						

EXAMINER	· · · · · · · · · · · · · · · · · · ·			DATE CON	SIDERED		

Fo	rm PT	O-1449 Modif	ied	Docket No. ISIS-5300	Applica 10/701,	ation No. ,265	
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office			Applicant Brenda F. Baker, et al.			
				Filing Date November 4, 2003	Group 1635		
		, , , , ,		Confirmation No. 7033			
		1	U. S. PATENT	Γ DOCUMENTS			
Examiner Initial		Document No.	Date	Name		Class	Subclass
	156	3,687,808	8/29/72	Merigan, et. al.		195	28
	157	5,013,830	5/7/91	Ohtsuka, et al.		536	27
	158	5,023,243	6/11/91	Tullis		514	44
	159	5,130,302	7/14/92	Spielvogel, et al.		514	45
	160	5,142,047	8/25/92	Tullis		514	44
	161	5,149,797	9/22/92	Pederson, et al.		536	27
	162	5,177,198	1/5/93	Spielvogel, et al.		514	45
	163	5,223,618	6/29/93	Cook, et al.		544	276
	164	5,235,033	8/10/93	Summerton, et al.		528	391
	165	5,256,775	10/26/93	Froehler		536	25.6
	166	5,264,562	11/23/93	Matteucci		536	23.1
	167	5,264,564	11/23/93	Matteucci		536	23.1
	168	5,359,044	10/25/94	Cook, et al.		536	23.1
	169	5,366,878	11/22/94	Pederson, et al.		435	91.3
	170	5,378,825	1/3/95	Cook, et al.		536	25.34
	171	5,457,191	10/10/95	Cook, et al.		536	27.13
	172	5,459,255	10/17/95	Cook, et al.		536	27.13
EXAMINE	R	*	. •	DATE CONSIDER	RED		

Fo	rm PT	O-1449 Modifie	d	Docket No. Application No. ISIS-5300 10/701,265			
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office			Applicant Brenda F. Baker, et al.			
				Filing Date November 4, 2003	Group 1635		
				Confirmation No. 7033			
		U. \$	S. PATENT	DOCUMENTS	l .		
Examiner Initial		Document No.	Date	Name		Class	Subclass
	173	5,466,786	11/14/95	Buhr, et al.		536	26.26
	174	5,476,925	12/19/95	Letsinger, et al.		536	23.1
	175	5,484,908	1/16/96	Froehler, et al.		536	24.31
	176	5,506,351	4/9/96	McGee		536	55.3
	177	5,514,786	5/7/96	Cook, et al.			
	178	5,386,023	1/31/95	Sanghvi, et al.		536	25.3
	179	5,489,677	2/6/96	Sanghvi, et al.		536	22.1
	180	5,539,083	7/23/96	Cook, et al.		530	333
	181	5,506,337	4/9/96	Summerton, et al.		528	391
	182	5,403,711	4/4/95	Walder, et al.		435	6
	183	5,508,270	4/16/96	Baxter, et al.		514	47
	184	4,373,071	02/08/83	Itakura		525	375
	185	4,401,796	08/30/83	Itakura		525	340
	186	4,469,863	9/4/84	Ts'o., et al.		536	27
	187	4,507,433	3/26/85	Miller, et al.		525	54.11
	188	4,812,512	3/14/89	Buendia, et al.		525	54.11
	189	4,908,405	3/13/90	Bayer, et al.		525	61
	190	5,391,667	2/21/95	Dellinger		526	264
EXAMINE	R			DATE CONSIDER	RED		

Fo	rm PT	O-1449 Modifi	ed	Docket No. ISIS-5300	Applica 10/701,	ation No. 265		
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)				Applicant Brenda F. Baker, et al.			
	U.S. Department of Commerce Patent and Trademark Office			Filing Date November 4, 2003	Group 1635			
			Confirmation No. 7033					
		U	. S. PATENT	DOCUMENTS				
Examiner Initial		Document No.	Date	Name		Class	Subclass	
	191	5,519,134	5/21/96	Acevedo, et al.		544	243	
	192	5,614,617	3/25/97	Cook, et al.		536	23.1	
	193	5,962,425	10/05/99	Walder, et al.		514	44	
	194	5,804,683	09/08/98	Usman et al.		536	25.31	
	195	5,891,683	04/06/99	Usman et al.		435	91.31	
	196	5,220,007	06/15/93	Pederson, et al.		536	23.1	
	197	5,491,133	02/13/96	Walder, et al.		514	44	
	198	5,565,350	10/15/96	Kmiec		435	172.3	
	199	5,623,065	04/22/97	Cook, et al.		536	23.1	
	200	5,652,355	07/29/97	Metelev, et al.		536	24.5	
	201	5,652,356	07/29/97	Agrawal		536	245	
	202	5,700,922	12/23/97	Cook		536	23.1	
	203	5,750,669	05/12/98	Rösch, et al.		536	24.3	
	204	5,837,852	11/17/98	Chung, et al.		536	24.5	
	205	5,898,031	04/27/99	Crooke, et al.		435	172.3	
EXAMINE	R			DATE CONSIDER	RED			

Fo	rm PT	O-1449 Modifi	ed	Docket No. ISIS-5300	Application 1 10/701,265	No.		
	List of Patent and Publications Cited by Applicant (Use several sheets if necessary)				Applicant Brenda F. Baker, et al.			
U. P	U.S. Department of Commerce Patent and Trademark Office			Filing Date November 4, 2003	Group 1635			
				Confirmation No. 7033			,	
,	•	U	. S. PATENT	T DOCUMENTS				
Examiner Initial		Document No.	Date	Name	Cla	ss Sube	class	
	206	6,107,094	08/22/00	Crooke	435	455		
-	207	6,117,657	09/12/00	Usman, et al.	435	91.3	1	
· · · · · · · · · · · · · · · · · · ·	208	6,262,036 B1	07/17/01	Arnold, Jr., et al.	514	44		
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EXAMINE	R			DATE CONSIDER	RED			

Application No. Docket No. Form PTO-1449 Modified 10/701,265 ISIS-5300 List of Patent and Publications **Applicant** Cited by Applicant Brenda F. Baker, et al. (Use several sheets if necessary) U.S. Department of Commerce Filing Date Group . Patent and Trademark Office November 4, 2003 1635 Confirmation No. 7033

FOREIGN PATENT DOCUMENTS

Examiner					Translation		
Initial		Document No.	Date	Country	YES	NO	
	209	WO 92/20822	11/26/92	PCT			
	210	WO 92/20823	11/26/92	PCT			
	211	WO 92/22651	12/23/92	PCT			
	212	WO 94/02499	02/03/94	PCT			
	213	WO 94/02501	02/03/94	PCT			
	214	WO 94/17093	08/04/94	PCT			
	215	339,842	11/02/89	EPO			
	216	2-264792	10/29/90	Japan			
	217	WO 92/07065	04/30/92	PCT			
	218	WO 99/32619	7/1/99	PCT		X	
	219	WO 00/44895	08/03/00	PCT	X abstract		
	220	WO 00/44914	08/03/00	PCT			
	221	WO 00/49035	08/24/00	PCT			
	222	WO 00/63364	10/26/00	PCT			
	223	WO 01/29058	04/26/01	PCT			
	224	WO 01/36641 A2	05/25/01	PCT			
EXAMINE	R			DATE CONSIDERED			

Application No. Docket No. Form PTO-1449 Modified 10/701,265 ISIS-5300 List of Patent and Publications **Applicant** Cited by Applicant Brenda F. Baker, et al. (Use several sheets if necessary) U.S. Department of Commerce Filing Date Group Patent and Trademark Office November 4, 2003 1635 Confirmation No. 7033 FOREIGN PATENT DOCUMENTS Examiner Translation **Country** Document No. **Date** YES Initial NO 225 WO 01/36646 A1 05/25/01 **PCT** 226 WO 01/48183 A2 07/05/01 **PCT** 227 WO 01/75164 A3 10/11/01 **PCT**

DATE CONSIDERED

EXAMINER